



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Syken et al.	Group Art Unit: 1632
Serial No.: 09/908,992	Examiner: Li, Q.
Filing Date: July 19, 2001	Attorney Docket No.: HMV-054.01
For: <i>Methods and Reagents to Regulate Apoptosis</i>	

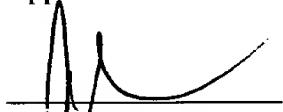
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22312-1450

Declaration of J. Syken and K. Münger under 37 C.F.R. § 1.132

Sir:

1. We, Joshua Syken, a citizen of the United States, residing at 19 Goldsmith Street, Jamaica Plain, Massachusetts and Karl Münger, a citizen of the Switzerland, residing at 33 Goddard Street, Newton, Massachusetts, hereby declare as follows:
2. I, Joshua Syken, Ph.D., am a Postdoctoral fellow, Department of Neurobiology, Harvard Medical School, Boston, Massachusetts. A copy of my curriculum vitae and list of publications are attached hereto as Exhibit A.
3. I, Karl Münger, Ph.D., am an Associate Professor, Department of Pathology, Harvard Medical School, Boston, Massachusetts. A copy of my resume and list of publications are attached hereto as Exhibit B.
4. We are co-inventors in the above-referenced patent application.
5. We understand that the publication Syken et al. (Proc. Natl. Acad. Sci. U.S.A. 96:8499-8504 (1999)) was cited against the above-referenced patent application.
6. We are the sole inventors of the experimental work described in Syken et al, *supra*.
7. Dr. Tali De-Medina, Ph.D., coauthor of Syken et al., *supra*, is not a co-inventor in the above-referenced application. Dr. De-Medina performed experiments confirming our initial observation that Tid1S localized to the mitochondria. Accordingly, Dr. De-Medina did not contribute to our invention as set forth in this patent application.
8. We declare that all statements made herein of our knowledge are true and that all statements made on information and belief are believed to be true; and further, that these

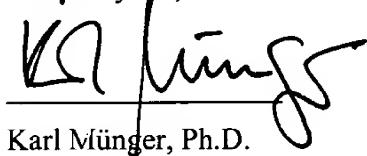
statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.



Joshua Syken, Ph.D.

6/9/03

Date



Karl Münger, Ph.D.

6/9/03

Date

Josh Syken, Ph.D.
19 Goldsmith St.
Jamaica Plain, MA 02130

Education/Research Experience

1992-1995
B.S., Purchase College, Purchase NY
Advisor: Dr. Elysse Craddock

1995-1999
Ph.D., Harvard Medical School
Advisor: Dr. Karl Munger
Thesis: TID1 Encodes Two Mitochondrial Modulators of Apoptosis with Opposing Functions

2000-Present
Postdoctoral fellow
Harvard Medical School
Advisor: Dr. Carla Shatz

Awards and Honors

1992 - CRC Chemistry Award, Purchase College
1992-1995 - William D. Schlutow Scholarship for Excellence in Biology,
Purchase College.
1995 - Purchase College Presidents Achievement Award
1995 - Suma Cum Laude, Purchase College
1997-1999 - Ryan Fellow, Harvard Medical School
2000-Present - NIH NRSA Postdoctoral Fellowship

Publications

Schilling B, De-Medina T, Syken J, Vidal M, Munger K. 1998. A novel human DnaJ protein, hTid-1, a homolog of the Drosophila tumor suppressor protein Tid56, can interact with the human papillomavirus type 16 E7 oncoprotein.
Virology. 1998 247(1):74-85

Syken J, De-Medina T, Munger K., 1999
TID1, a human homolog of the Drosophila tumor suppressor l(2)tid, encodes two mitochondrial modulators of apoptosis with opposing functions.
Proc Natl Acad Sci U S A. 96(15):8499-504

Syken, J., Macian, F., Agarwal, S., Rao, A., Munger, K., 2003. TID1, a Mammalian Homolog of the Drosophila Tumor Suppressor lethal(2) tumorous imaginal discs Regulates Activation-Induced Cell Death in Th2 Cells. *Oncogene*, In Press.

CURRICULUM VITAE

PART I: General Information

DATE PREPARED: June 5, 2003

Name: Karl Münger

Office Address: Department of Pathology
Harvard Medical School
200 Longwood Ave.
Boston, MA 02115-5701
617-432-2878 (tel)

Home Address: 33 Goddard Street
Newton, MA 02461-1917

E-Mail: karl_munger@hms.harvard.edu **FAX:** 617-423-0426

Place of Birth: Zürich, Switzerland

Education:

1981 B.Sc. (Biochemistry), University of Zürich, Switzerland
1986 Ph. D. (Biochemistry), University of Zürich, Switzerland

Postdoctoral Training:

1986-1990 Viral Oncology, Laboratory of Tumor Virus Biology, National Cancer Institute, NIH, Bethesda, MD

Professional Appointments:

1990-1993 Visiting Associate, Laboratory of Tumor Virus Biology, National Cancer Institute, NIH, Bethesda, MD

1993-present Member, Board of Tutors in Biochemical Sciences, Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA.

1993 –1998 Assistant Professor, Department of Pathology, Harvard Medical School, Boston, MA

1998-present Associate Professor, Department of Pathology, Harvard Medical School, Boston, MA

Other Professional Positions and Major Visiting Appointments:

1995 Consultant, WHO/IARC Working Group on Human Papillomaviruses

1995-1996 Faculty Member, Histopathobiology of Neoplasia Workshop, organized by the American Association for Cancer Research

1996 Visiting Professor, Department of Biology, University of Padua, Italy

1999 Consultant, Boston BioProducts, Inc., Ashland, MA

1999 Consultant, McKinsey and Company

2001-date Consultant, National Toxicology Program, Evaluation of HPV as a Carcinogen

2002 Consultant, Pharmacia-Upjohn Company, Kalamazoo, MI.

2002 Faculty Member, Pathobiology of Cancer Workshop, organized by the American Association for Cancer Research

2002-present Consultant, Arbor Vita Corporation, Sunnyvale CA

Major Committee Assignments:

1996 Temporary Member, Experimental Virology Study Section, National Institutes of Health

1996 Scientific Committee, 15th International Papillomavirus Workshop, Queensland, Australia 1996

1997 Temporary Member, Experimental Virology Study Section, National Institutes of Health

1998 Chairman, Viral Oncology Section, Program Committee, American Association for Cancer Research, Annual Meeting.

1998 Organizing Committee, International Conference on Small DNA Tumorviruses, Madison, WI.

1998 Member, NIH Special Emphasis Panel (ZRG5 EVR-01) Study Section

1998 Member, NIH Site Visit Committee for Program Project 1 P01 DE2704-01.

1998 Member, NIH Site Visit Committee for Program Project 1 P50 DC00203-15A1

1998-2001 Cancer Research Campaign (UK), Outside Reviewer

1999 Scientific Program Committee, 17th International Papillomavirus Workshop, Charleston, SC.

1999 Grant Reviewer, National Science Foundation of Austria

1998 Member, NIH Special Emphasis Panel (DE 98-008)

1999 Temporary Member, NIDCR Special Emphasis Panel

2000-2001 Review Board, NIGM/NIH Intramural Postdoctoral Fellowship Program (PRAT Fellowships)

2000, 2003 Grant Reviewer, Dutch Cancer Society.

2000 Organizing Committee, International Conference on Small DNA Tumorviruses, Madison, WI.

2000-date Member NIDCR Special Review Panel.

2000-date Tenure Reviewer for Tufts University (2), Case Western University, Cleveland OH, University of Massachusetts, The Hebrew University of Jerusalem (Israel)

2000-2004 Regular Member, NIH Study Section "Virology".

2001, 2003 Grant Reviewer, National Science Foundation, Austria.

2001 Grant Reviewer, Italian Association for Cancer Research

2001 Scientific Program Committee, 19th International Papillomavirus Workshop, Florianopolis, Brazil

2002 Grant Reviewer, Ohio Cancer Research Associates.

2002 Grant Reviewer, Sass Fellowship Foundation

2002, 2003 Grant Reviewer, Department of Veterans Affairs

2002 Member, NIDCD Special Review Panel 020628.

2002 Organizing Committee, International Conference on Small DNA Tumorviruses, Madison, WI.

2002 Grant Reviewer, Research Management Group, Linthicum Heights, MD

2002 Grant Reviewer, Cancer Research UK

2003 Nomination Committee, NIGM/NIH Intramural Postdoctoral Fellowship Program (PRAT Fellowships)

2003 Member, Viral Oncogenesis and Mechanisms Section of the Cellular, Molecular, and Tumor Biology Subcommittee of the Program Committee for the Annual Meeting of the American Association for Cancer Research.

2003 Member, NIH Site Visit Committee for Program Project 1 P01 CA16038-31

2004 Scientific Committee, 21st International Papillomavirus Conference

Professional Societies:

Swiss Society for Biochemistry
American Society for Microbiology
American Association for Cancer Research
American Society for Investigative Pathology
Boston Cancer Research Association (Massachusetts Section of the American Association for Cancer Research), Vice President 1997-1998; President 1998-1999
International Papillomavirus Society

Community Service Related to Professional Work:

2001 Mentor, Outside Researchers Session, Excellence Through Diversity Initiative, Doctoral Scholars Program, New England Board of Higher Education.
2003 Mentor, Minorities in Cancer Research Council of the AACR, Symposium: "Navigating the Road to a Successful Career in Cancer Research"

Editorial Boards:

1995-present Journal of Virology
1998-present Virology
2001-present Cancer Research; Associate Editor
2001-present Cancer Biology & Therapy; Associate Editor
2003-present Molecular Cancer

Ad hoc reviewer for: Am. J. Pathol., Biochemistry, Biochem. Biophys. Acta, Br. J. Cancer., Cancer, Cancer Detection and Prevention, Cancer Invest., Cell, Cell Death Diff., Cell Growth Diff., Clin. Canc. Res., EMBO J., Exp. Cell Res., Gene, Genes & Development, Genes, Chromosomes and Cancer, Gynecol. Oncol., Int. J. Cancer, IUBMB Life., J. Cell Science., J. Clin. Invest., J. Clin. Oncol., J. Exp. Med., J. Immunol., J. Natl. Canc. Inst., Mol. Cell Biol., Mol. Pharmacol., Microbiol. Mol. Biol. Reviews., Nature, Nature Cell Biology, Nature Medicine, Nucl. Acids Res., Oncogene, Oncol. Res., Proc. Natl. Acad. Sci. USA, Science, Trends in Microbiology, Virus Res.

Awards and Honors:

1986-1988 John E. Fogarty Postdoctoral Fellowship
1989 Advanced Training Fellowship, Swiss National Science Foundation
1990 Dr. Ernst Th. Jucker Award for Experimental Cancer Research, Zürich, Switzerland
1996-1998 Junior Faculty Research Award, American Cancer Society
1998-2000 Ludwig Scholar

Funding

Past:

1/94-12/94 Funds for Discovery; PI; "Disruption of dimer formation as a strategy to inactivate the HPV E7 oncoprotein."
1/94-12/94 Milton Fund; PI; "Protein domains governing the transformation function of the HPV E7 oncoprotein."
1/94-12/98 American Cancer Society; PI; "Characterization of cellular factors associated with the HPV E7 protein" (#VM97; #RPG-94-011-04-VM).

1/95-12/97 Council for Tobacco Research; PI; "Viral oncoproteins as probes to study cellular growth regulation" (#3859).

1/96-12/98 American Cancer Society; PI; "The role of HPV E7 in cervical carcinogenesis" (JFRA-597)

6/97-5/98 National Institutes of Health; PI; "The role of basic helix-loop-helix (bHLH) proteins in epithelial cell proliferation and differentiation"; Pilot and Feasibility Project Grant; P30 AR42689 (T.S. Kupper, PI).

4/99-3/00 GLAXO-WELLCOME Co., PI; "Alteration of Cellular Signal Transduction Pathways by the Human Papillomavirus E7 Oncoprotein"; Industry-sponsored Research Grant.

7/99-6/01 Hoechst Marion Roussel Co., "Modulation of TID1 During T-Cell Activation: Implications for Activation Induced Cell Death" Industry sponsored Research Grant.

4/98-3/03 Project leader; National Institutes of Health; "Cell cycle dysregulation in oral cancer"; Program Project Grant P01 DE012467 (David T. Wong, PI).

Current:

4/96-6/05 Principal Investigator: National Cancer Institute/National Institutes of Health; "Biological activity of HPV E7 in human epithelial cells" (R01 CA66980).

9/02-6/05 Principal Investigator: National Cancer Institute/National Institutes of Health; "Biological activity of HPV E7 in human epithelial cells"- Competitive Supplement (3R01CA066980-7S1)

2/00-1/05 Principal Investigator: National Cancer Institute/National Institutes of Health; "Modulation of Host Cell Apoptotic Responses by HPV E7" (R01 CA81135).

10/01-9/06 Project Co-investigator; National Heart, Lung, and Blood Institute/National Institutes of Health; "Adhesion molecules in transfusion biology" Program Project Grant 2P01 HL56949 (Denisa Wagner, P.I.).

7/02-6/03 Co-investigator: Stewart Trust; "Identification of cellular markers of human cervical preneoplasia by Serial Analysis of Gene Expression (SAGE)"

12/02-11/04 Principal Investigator: Astra-Zeneca; "Tripeptidyl transferase II and c-myc induced centrosome mediated genomic instability"

6/03-5/05 Co-Principal Investigator: CYTYC Corporation; "Cellular markers of cervical neoplasia"

7/03-11/07 Project Co-investigator: National Cancer Institute/National Institutes of Health; "Spectroscopic imaging and diagnosis of neoplasia" Bioengineering Research Partnership CA097966-01; (Michael Feld, MIT, P.I.)

Bibliography

Original Articles:

1. Münger K, Lerch K, Tschierpe HJ. Metal accumulation in *Agaricus bisporus*: influence of Cd and Cu on growth and tyrosinase Activity. *Experientia* 38:1039-1041, 1982.
2. Münger K, Germann UA, Beltramini M, Niedermann D, Baitella-Eberle G, Kägi JHR, Lerch K. (Cu/Zn) Metallothioneins from fetal bovine liver: chemical and spectroscopic properties. *J. Biol. Chem.* 260:10032-10038, 1985.
3. Münger K, Germann UA, Lerch K. Isolation and structural organization of the *Neurospora crassa* copper metallothionein gene. *EMBO J.* 4:2665-2668, 1985.
4. Münger K, Lerch K. Copper metallothionein from the fungus *Agaricus bisporus*: chemical and spectroscopic properties. *Biochemistry* 24:6751-6756, 1985.
5. Münger K, Germann UA, Lerch K: The *Neurospora crassa* copper metallothionein gene: regulation of expression and chromosomal location. *J. Biol. Chem.* 262:7363-7367, 1987.
6. Moser R, Frey S, Münger K, Hehlgans T, Klauser S, Langen H, Winnacker E-L, Mertz R, Gutte B. Expression of the synthetic gene of an artificial DDT-binding polypeptide in *E. coli*. *Protein Engineering* 1:339-347, 1987.
7. Münger K, Lerch K. Peptide mapping of vertebrate and invertebrate metallothioneins. *Inorganica Chimica Acta* 151:11-13, 1988.
8. Phelps WC, Yee CL, Münger K, Howley PM. The human papillomavirus type 16 E7 gene encodes transactivation and transformation functions similar to adenovirus E1a. *Cell* 53:339-347, 1988.
9. Beltramini M, Giacometti GM, Salvato B, Giacometti G, Münger K, Lerch K. Luminescence emission from *Neurospora* copper metallothionein: Time-resolved Studies. *Biochem. J.* 260:189-193, 1989.
10. Dyson N, Howley PM, Münger K, Harlow, E. The human papillomavirus type 16 E7 oncoprotein is able to bind the retinoblastoma gene product. *Science* 243:934-937, 1989.
11. Münger K, Phelps WC, Bubb V, Howley PM, Schlegel R. The E6 and E7 genes of the human papillomavirus type 16 together are necessary and sufficient for transformation of primary human keratinocytes. *J. Virol.* 63:4417-4421, 1989.
12. Münger K, Werness BA, Dyson N, Phelps WC, Harlow E, Howley PM. Complex formation of human papillomavirus E7 proteins with the retinoblastoma tumor suppressor gene product. *EMBO J.* 8:4099-4105, 1989.
13. Pietenpol JA, Stein RW, Moran E, Yaciuk P, Schlegel R, Lyons RM, Pittelkow MR, Münger K, Howley PM, Moses HL. TGF β 1 inhibition of c-myc transcription and growth in keratinocytes is abrogated by viral transforming proteins with pRB binding domains. *Cell* 61:777-785, 1990.
14. Münger K, Yee CL, Phelps WC, Pietenpol JA, Moses HL, Howley PM. Biochemical and biological differences between E7 oncoproteins of the high and low risk HPVs are determined by amino terminal sequences. *J. Virol.* 65:3943-3948, 1991.

15. Scheffner M, Münger K, Byrne JC, Howley PM. The state of the p53 and retinoblastoma genes in human cervical carcinoma cell lines. *Proc. Natl. Acad. Sci. USA* 88:5523-5527, 1991.
16. Phelps WC, Bagchi S, Barnes J, Raychaudhuri P, Krause V, Münger K, Howley PM, Nevins JR. Analysis of trans-activation by HPV-16 E7 and adenovirus 12S E1A suggests a common mechanism. *J. Virol.* 65:6922-6930, 1991.
17. Pietenpol JA, Münger K, Howley PM, Stein RW, Moses HL. A factor-binding element in the human c-myc promoter involved in transcriptional regulation by transforming growth factor β -1 and by the retinoblastoma gene product. *Proc. Natl. Acad. Sci. USA* 88:10227-10231, 1991.
18. Phelps WC, Münger K, Yee CL, Barnes JA, Howley PM. Structure-function analysis of the HPV16 E7 oncoprotein. *J. Virol.* 66:2418-2427, 1992.
19. Münger K, Pietenpol JA, Pittelkow MR, Holt JT, Moses HL. Transforming growth factor β 1 regulation of c-myc expression, pRB phosphorylation, and cell cycle progression in keratinocytes. *Cell Growth & Differentiation* 3:291-298, 1992.
20. Chellappan S, Kraus VB, Kroger B, Münger K, Howley PM, Phelps WC, Nevins JR. E1A, T antigen and E7 share the capacity to disrupt the E2F-Rb interaction: implications for viral replication and the generation of human tumors. *Proc. Natl. Acad. Sci. USA* 89:4549-4553, 1992.
21. Heck DV, Yee CL, Howley PM, Münger K. Efficiency of binding the retinoblastoma protein correlates with the transforming capacity of the E7 oncoproteins of the human papillomaviruses. *Proc. Natl. Acad. Sci. USA* 89:4442-4446, 1992.
22. Scheffner M, Münger K, Huibregtse JM, Howley PM. Targeted degradation of the retinoblastoma protein by a fusion of the human papillomavirus E6 and E7 oncoproteins. *EMBO J.* 11:2425-2431, 1992.
23. Dyson N, Guida P, Münger K, Harlow E. Homologous sequences in adenovirus E1A and human papillomavirus E7 proteins mediate interaction with the same set of cellular proteins. *J. Virol.* 66:6893-6902, 1992.
24. Wu EW, Clemens KE, Heck DV, Münger K. The human papillomavirus E7 oncoprotein and the cellular transcription factor E2F bind to separate sites on the retinoblastoma tumor suppressor protein. *J. Virol.* 67:2402-2407, 1993.
25. Arbeit JM, Münger K, Howley PM, Hanahan D. Neuroepithelial carcinomas in mice transgenic with human papillomavirus Type 16 E6/E7 ORFs. *Am. J. Pathol.* 142:1187-1197, 1993.
26. Arbeit JM, Münger K, Howley PM, Hanahan D. Progressive squamous epithelial neoplasia in K14-HPV16 transgenic mice. *J. Virol.* 68:4358-4368, 1994.
27. Brokaw JL, Yee CL, Münger K. A mutational analysis of the amino terminal domain of the human papillomavirus type 16 E7 oncoprotein. *Virology* 205:603-607, 1994.
28. Clemens K, Brent R, Gyuris J, Münger K. Dimerization of the HPV E7 oncoprotein in vivo. *Virology* 241:289-293, 1995.

29. Timmermann S, Hinds P, Münger K. Elevated activity of cyclin-dependent kinase 6 in oral carcinomas. *Cell Growth & Differentiation* 8:361-370, 1997.
30. Jones DL, Münger K. Analysis of the p53- mediated G1 growth arrest pathway in cells expressing the human papillomavirus type 16 E7 oncoprotein. *J. Virol.* 71:2905-2912, 1997
31. Oettgen P, Alani RM, Barcinski M, Akbarali Y, Boltax J, Brown L, Kunsch C, Münger K, Liberman TA. Isolation and characterization of a novel epithelial-specific transcription factor, ESE-1, a member of the ets family. *Mol. Cell. Biol.* 17:4419-4433, 1997.
32. Jones DL, Alani RM, Münger, K. The human papillomavirus E7 oncoprotein can uncouple cellular differentiation and proliferation in human keratinocytes by abrogating p21Cip1-mediated inhibition of cdk2. *Genes & Development* 11:2101-2111, 1997.
33. Mavromatis KO, Jones DL, Muherjee R, Yee C, Grace M, Münger K. The carboxyl terminal zinc-binding domain of the human papillomavirus E7 protein can be functionally replaced by the homologous sequences of the E6 protein. *Virus Research* 52:109-118, 1997.
34. Thompson DA, Belinsky G, Chang TH-T, Jones DL, Schlegel R, Münger K. The human papillomavirus-16 E6 oncoprotein decreases the vigilance of mitotic checkpoints. *Oncogene* 15:3025-3036, 1997.
35. Jones DL, Thompson, DA, Münger K. Destabilization of the pRB tumor suppressor protein and stabilization of p53 contribute to HPV type 16-induced apoptosis. *Virology* 239:97-107, 1997.
36. Schilling B, De-Medina T, Syken J, Vidal M, Münger K. A novel human DnaJ protein, hTid-1, a homolog of the Drosophila tumor suppressor protein Tid56, can interact with the human papillomavirus type 16 E7 oncoprotein. *Virology* 247:74-85, 1998.
37. Alani RM, Hasskarl J, Münger K. Alterations of cyclin-dependent kinase 2 function during differentiation of primary human keratinocytes. *Molecular Carcinogenesis* 23:226-233, 1998.
38. Timmermann S, Hinds PH, Münger K. Reexpression of endogenous p16INK4a in oral squamous cell carcinoma lines by 5-aza-2'-deoxycytidine induces a senescence-like state. *Oncogene* 17:3445-3453, 1998.
39. Jones DL, Thompson DA, Suh-Bürgmann E, Grace M, Münger K. Expression of the HPV E7 oncoprotein mimics but does not evoke a p53-dependent DNA damage response pathway. *Virology*, 258:406-414, 1999.
40. Syken J, De-Medina T, Münger K. hTid-1, the human homolog of the Drosophila tumor suppressor Tid56, is a mitochondrial regulator of apoptosis. *Proc. Natl. Acad. Sci. USA* 96:8499-8506, 1999.
41. Alani RM, Hasskarl J, Grace M, Hernandez MC, Israel MA, Münger K. Immortalization of primary human keratinocytes by the helix-loop-helix protein, Id1. *Proc. Natl. Acad. Sci. USA* 96:9637-9641, 1999.
42. Oettgen P, Kas K, Dube A, Gu X, Grall F, Thamrongsak U, Akbarali Y, Finger E, Boltax J, Endress G, Münger K, Kunsch C, Libermann TA. Characterization of ESE-2, a novel

ESE-1-related ets transcription factor that is restricted to glandular epithelium and differentiated keratinocytes. *J. Biol. Chem.* 274:29439-29452, 1999.

43. Park JS, Boyer S, Mitchell K, Gilfor D, Birrer M, Darlington G, El Deiry W, Firestone GL, Münger K, Band V, Fisher PB, Dent P. Expression of human papilloma virus E7 protein causes apoptosis and inhibits DNA synthesis in primary hepatocytes via increased expression of p21(Cip-1/WAF1/MDA6). *J Biol Chem* 275:18-28, 2000.

44. Duensing S, Lee LY, Duensing A, Basile J, Piboonnnyom, S, Münger K. The human papillomavirus type 16 E6 and E7 oncoproteins cooperate to induce mitotic defects and genomic instability by uncoupling centrosome duplication from the cell division cycle. *Proc. Natl. Acad. Sci USA* 97:10002-10007, 2000.

45. Duensing S, Duensing A, Crum, CP, Münger K: Human papillomavirus type 16 E7 oncoprotein induced abnormal centrosome synthesis is an early event in the evolving malignant phenotype, *Cancer Research* 61:2356-2360, 2001.

46. Thompson DA, Zacny V, Belinsky GS, Classon M, Jones DL, Schlegel R, Münger K: The HPV E7 oncoprotein abrogates Tumor Necrosis Factor-a-mediated pro-caspase 8 activation and apoptosis in normal human fibroblasts, *Oncogene* 20:3629-3640, 2001

47. Basile JR, Zacny V, Münger K: The cytokines TNF-a and TRAIL differentially modulate proliferation and apoptotic pathways in human keratinocytes expressing the HPV-16 E7 oncoprotein, *J. Biol. Chem.* 276:22522-22528, 2001.

48. Keating JT, Cviko A, Riethdorf S, Riethdorf L, Quade BJ, Sun D, Duensing S, Sheets EE, Munger K, Crum CP: Ki-67, cyclin E and p16INK4A are complimentary surrogate biomarkers for human papillomavirus-related cervical neoplasia, *Am J Surg Pathol* 25:884-891, 2001.

49. Gonzalez SL, Stremlau M, He X, Basile JR, Münger K: Degradation of the retinoblastoma tumor suppressor by the human papillomavirus type 16 E7 oncoprotein is important for functional inactivation and is separable from proteasomal degradation of E7, *J. Virol.* 75:7583-7591, 2001

50. Duensing S, Duensing A, Flores ER, Do A, Lambert PF, Münger K. Centrosome abnormalities and genomic instability by episomal expression of human papillomavirus type 16 in raft cultures of human keratinocytes, *J. Virol.* 75:7712-7716, 2001

51. Jiang X, Wilford C, Duensing S, Münger K, Jones G, Jones D. Participation of Survivin in mitotic and apoptotic activities of normal and tumor-derived cells, *J Cell Biochem* 83:342 -354, 2001

52. Piboonnnyom S, Timmermann S, Hinds P, Münger K: Aberrations in the MTS1 tumor suppressor locus in oral squamous cell carcinoma lines preferentially affect the INK4A gene and result in increased cdk6 activity, *Oral Onc* 38:179-186, 2002

53. Eichten A, Westfall M, Pietenpol JA, Münger K: Stabilization and functional impairment of the tumor suppressor p53 by the human papillomavirus type 16 E7 oncoprotein, *Virology* 295:74-85, 2002

54. Duensing S, Münger K: The human papillomavirus type 16 E6 and E7 oncoproteins independently induce numerical and structural chromosome instability, *Cancer Research* 62:7075-7082, 2002
55. Piboonniyom S, Duensing S, Swilling NW, Hasskarl J, Hinds PW, Münger K: Abrogation of the retinoblastoma tumor suppressor checkpoint during keratinocyte immortalization is not sufficient for induction of centrosome-mediated genomic instability, *Cancer Research* 63: 476-483, 2003
56. Genther SM, Sterling S, Duensing M, Münger K, Sattler C, Lambert PF: A quantitative role of the human papillomavirus type 16 E5 gene during the productive stage of the viral life cycle, *Journal of Virology* 77:2832-2842, 2003.
57. Basile JR, Eichten A, Zacny V, Münger K: NF- κ B mediated induction of p21^{Cip1/Waf1} by tumor necrosis factor α induces growth arrest and cytoprotection in normal human keratinocytes, *Molecular Cancer Research* 1: 262-270, 2003.
58. Syken J, Macian F, Agarwal S, Rao, A, Münger, K: TID1, a Mammalian Homolog of the Drosophila Tumor Suppressor lethal(2) tumorous imaginal discs Regulates Activation-Induced Cell Death in Th2 Cells, *Oncogene* 22: in press 2003.
59. Kleine-Lowinsky K, Rheinwald JG, Fichorova RN, Anderson DJ, Basile JR, Münger K, Daly CM, Rösl F, Rollins BJ: Selective suppression of monocyte chemoattractant protein-1 (MCP-1) expression by human papillomavirus E6 and E7 oncoproteins in human cervical epithelial and epidermal cells, *Int. J. Cancer* 106: in press 2003
60. Riley R, Duensing S, Brake T, Münger K, Lambert PF, Arbeit JM: Dissection of human papillomavirus E6 and E7 function in transgenic mouse models of cervical carcinogenesis, submitted
61. Basile JR, Zacny V, Eichten A, Münger K: TRAIL/APO2L signaling in primary human keratinocytes does not involve rapid anti-apoptotic NF- κ B activation, submitted
62. Balsitis SJ, Sage J, Duensing S, Munger K, Jacks T, Lambert PF. Recapitulation of the effects of HPV-16 E7 oncogene on mouse epithelium by somatic Rb deletion and detection of pRb-independent effects of E7 in vivo, submitted

Proceedings of Meetings:

1. Münger K, Germann UA, Lerch K. Isolation and Regulation of Expression of the *Neurospora crassa* Copper Metallothionein Gene. *Experientia Suppl.* 52:393-400, 1987.
2. Beltramini M, Münger K, Germann UA, Lerch K. Luminescence emission from the Cu(I) thiolate complex in metallothioneins. *Experientia Suppl.* 52:237-242, 1987.
3. Münger K, Germann UA, Beltramini M, Kupper U, Lerch K. *Neurospora* Copper Metallothionein: Molecular Structure and Gene Expression. *UCLA Symp. Mol. Cell. Biol.* 98:227-235, 1989.
4. Münger K, Phelps WC, Bubb V, Howley PM, Schlegel R. Keratinocyte transformation by the HPV-16 E6 and E7 genes progresses through two distinct morphological stages. *UCLA Symp. Mol. Cell. Biol.* 124:223-230, 1990.

5. Münger K, Phelps WC, Howley PM. Human papillomaviruses and neoplastic transformation. *Bristol Myers Cancer Symp.* 11:223-254, 1990.
6. Cowser LM, Münger K, Howley PM, Baker CC. The E6-E7 region of HPV-16 is sufficient for altered differentiation of human keratinocytes. *UCLA Symp. Mol. Cell. Biol.* 124:265-270, 1990.
7. Phelps WC, Münger K, Yee CL, Howley PM. Site directed mutagenesis of the HPV-16 E7 protein. *UCLA Symp. Mol. Cell. Biol.* 124:305-311, 1990.
8. Howley PM, Münger K, Werness BA, Phelps WC, Schlegel R. Molecular mechanisms of transformation by the human papillomaviruses. In: *Genetic basis for carcinogenesis: tumor suppressor genes and oncogenes* (AG Knudson Jr, et al, eds) Japan Sci. Soc. Press Tokyo/Taylor & Francis Ltd London 1990, pp 199-206.
9. Howley PM, Scheffner M, Huibregtse JM, Münger K. The oncoproteins encoded by the cancer associated human papillomaviruses target the products of the retinoblastoma and p53 tumor suppressor genes. *CSH Symp. Quant. Biol.* LVI:149-155, 1992.
10. Murphy CS, Pietenpol JA, Münger K, Howley PM, Moses HL. C-MYC and pRB: role in TGF β 1 inhibition of keratinocyte proliferation. *CSH Symp. Quant. Biol.* LVI:129-135, 1992.
11. Moses HL, Pietenpol JA, Münger K, Murphy CS, Yang EY. TGF β Regulation of epithelial cell proliferation: role of tumor suppressor genes. In: *multistage carcinogenesis* (CC Harris et al, eds) Japan Sci. Soc. Press, Tokyo/CRC Press, Boca Raton 1992, pp 183-195.
12. Howley PM, Münger K, Romanczuk H, Scheffner M, Huibregtse JM. Cellular targets of the oncoproteins encoded by the cancer associated human papillomaviruses. In: *Multistage carcinogenesis* (CC Harris et al, eds) Japan Sci. Soc. Press, Tokyo/CRC Press, Boca Raton 1992, pp 239-248.
13. Scheffner M, Münger K, Huibregtse JM, Mietz JA, Howley PM. Interaction of the HPV E6 and E7 oncoproteins with the tumor suppressor proteins p53 and pRB. In: *Precancerous lesions: a multidisciplinary approach* (Series: *Challenges of modern medicine*, 1993) (PA Marks, H Turler, R Weil, eds) Ares-Serono Symposia Publications, Rome Italy 1993, pp 177-189.
14. Münger K. The molecular biology of cervical cancer. *J. Cell. Biochem.* 23 (Suppl):55-60, 1995.
15. Human Papillomaviruses, IARC monographs on the evaluation of carcinogenic risks to humans; Volume 64. ISBN 92 832 1264 9. IARC/WHO Press, Lyon France 1995.
16. McBride AA, Androphy E, Münger K. Regulation of the papillomavirus E6 and E7 oncoproteins by the viral E1 and E2 proteins. In: *Viral regulatory structures and their degeneracy* (G Myers et al eds) Santa Fe institute studies in the science of complexity, vol XXVIII, Addison-Wesley 1998, pp 35-52
17. Münger K, Howley PM. Human Papillomavirus Immortalization and Transformation Functions. *Virus Res* 89:213-228, 2002.

18. Badizadegan K, Backman V, Boone CW, Crum CP, Dasari RR, Georgakoudi I, Keefe K, Munger K, Shapshay SM, Sheets EE, Feld MS. Spectroscopic diagnosis and imaging of invisible pre-cancer. *Faraday Discussions* No 126 "Applications of Spectroscopy to Biomedical Problems" in press 2003.

Reviews, Chapters and Editorials

1. Phelps WC, Münger K, Yee CL, Schlegel R, Howley PM. Human genital papillomaviruses: transcriptional regulation and transformation. In: *Common mechanisms of transformation by small DNA tumor viruses*, (LP Villareal, ed), ASM Publications, Washington DC 1989, pp 149-164.
2. Phelps WC, Yee CL, Münger K, Howley PM. Functional and sequence similarities between HPV16 E7 and adenovirus E1A. *Current Topics Microbiol. Immunol.* 144:153 - 166, 1989.
3. Münger K, Werness BA, Cowser LM, Phelps WC. Papillomaviruses and neoplastic transformation. In: *Encyclopedia of human biology* vol 5 (R Dulbecco, ed), Academic Press 1991, pp 635-643. Second edition has been published.
4. Werness BA, Münger K, Howley PM. The role of the human papillomavirus oncoproteins in transformation and carcinogenic progression. In: *Important advances in oncology* 1991 (VT DeVita Jr, S Hellman, S Rosenberg eds), J.B. Lippincott Company, Philadelphia PA 1991, pp 3-18.
5. Münger K, Scheffner M, Huibregtse JM, Howley PM. The interactions of the HPV E6 and E7 oncoproteins with tumor suppressor products. *Cancer Surveys* 12:197-217, 1992.
6. Münger K, Phelps WC. The human papillomavirus E7 protein as a transforming and transactivating factor. *Biochem. Biophys. Acta* 1155:111-123, 1993.
7. Scheffner M, Romanczuk H, Münger K, Huibregtse JM, Mietz JA, Howley PM. Functions of HPV proteins. *Current Topics Microbiol. Immunol.* 186:83-99, 1994.
8. Münger K. Host-viral gene interactions in cervical cancer. *Contemp. OB/GYN* 40:27-37, 1995.
9. Jones DL, Münger K. Interactions of the human papillomavirus E7 protein with cell cycle regulators. *Seminars in Cancer Biology* 7:327-337, 1996.
10. Alani RM, Münger K. Human papillomaviruses and associated malignancies. *Journal of Clinical Oncology* 16:330-337, 1998.
11. Alani RM, Münger K. Human papillomaviruses. *Science & Medicine* 5:28-35, 1998.
12. Howley PM, Münger K. Human papillomaviruses and squamous-cell carcinomas. In: *Microbes and malignancy* (JA Parsonnet, ed) Oxford University Press, New York/Oxford 1999, pp 157-179.
13. Münger K, Heselmeyer K. The molecular pathogenesis of cervical cancer: The role of human papillomaviruses. In: *Molecular pathology of early cancer* (S Srivastava et al, eds) IOS Press, Amsterdam 1999, pp 97-111.

14. Wong DTW, Münger K: Association of human papillomaviruses with a subgroup of head and neck squamous cell carcinoma. *J. Natl. Cancer Inst.* 92:675-677, 2000 (invited editorial)
15. Münger, K. Learning old tricks from new viruses. *Nature Med* 6:1091-1092, 2000 (invited News and Views article)
16. Duensing S, Münger K. Centrosome abnormalities, genomic instability and carcinogenic progression. *Biochim Biophys Acta* 1471:M81-M88, 2001.
17. Münger K, Basile JR, Duensing S, Eichten A, Gonzalez SL, Grace M, Zacny VL. Biological Activities and Molecular Targets of the Human Papillomavirus E7 Oncoprotein, *Oncogene* 20:7888-7898, 2001.
18. Todd R, Hinds PW, Munger K, Rustgi AK, Opitz OG, Suliman Y, Wong DT: Cell cycle dysregulation in oral cancer. *Crit. Rev. Oral Bio.* 13:51-56 2002.
19. Münger K: The role of human papillomaviruses in human cancers, *Frontiers in Biosciences* 7, d641-649, 2002
20. Hasskarl J, Münger K: Id Proteins - Tumor Markers or Oncogenes, *Cancer Biology & Therapy* 1:91-96, 2002
21. Münger K: Disruption of Oncogene-tumor suppressor networks during human carcinogenesis, *Cancer Investigation* 20:71-81, 2002
22. Münger K: Papillomaviruses In "Encyclopedia of Cancer", Second Edition (JR Bertino, ed) Academic Press, San Diego, vol 3:393-401 (2002)
23. Duensing S, Münger, K: Human papillomaviruses and centrosome duplication errors: Modeling the origins of genomic instability, *Oncogene* 21:6241-6448 (2002)
24. Münger K: Clefts, grooves and (small) pockets: The structure of the retinoblastoma tumor suppressor to its cellular target E2F unveiled. *Proc. Natl. Acad. Sci USA* 100:2165-2167, 2003 (invited commentary).
25. Duensing S, Münger, K: Centrosome abnormalities and genomic instability induced by human papillomavirus oncoproteins: In *Progress in Cell Cycle Research* vol 5 "Cell Cycle Regulators as Therapeutic Targets" 2003, pp383-391
26. Münger K: Oncoproteines virales: In "Papillomavirus Humains" (F Aubin, JL Pretot, C Mougin eds) in press 2003.
27. Duensing S, Münger K: Centrosomes, genomic instability, and cervical carcinogenesis, *Critical Reviews in Eukaryotic Gene Expression* 2003, in press.

Thesis:

Münger, K.: Chemical and Molecular Biological Studies on Copper Metallothioneins from Fungi. Zürich (Switzerland): University of Zürich, 1986.

Nonprint Material:

Halpern, AL, Münger K. HPV-16 E7: Correspondence between primary structure and biological properties. HPV Sequence Database, Los Alamos National Laboratory, 1995, pp III-58-III-73 (<http://hpv-web.lanl.gov/HPVOnLine.html#comp95>)

Patents:

“Method and kit for evaluating transformed cells.” US Patent 5736318; Issue date 04/07/98

“Methods and reagents to regulate apoptosis” Docket No.:HMV-054.60; filing date 7/19/00

“Methods of use of tripeptidyl peptidase II inhibitors as anticancer agents” Docket No: HU#2061; filing date 6/14/02